Review of 404 Patients with Gastrointestinal Fistulas

Impact of Parenteral Nutrition

PETER B. SOETERS,* AMIN M. EBEID, JOSEF E. FISCHER, M.D.†

From the Department of Surgery, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

This paper represents an extensive review, spanning 30 years of experience with 404 patients with gastrointestinal fistulas. It includes the first period (1945–1960) during the introduction of antibiotics, the second period (1960–1970) which saw rapid improvements in parasurgical care including, respiratory support, perfection of antibiotics, some introduction of nutritional support and improved monitoring, and the third period which saw the introduction of parenteral nutrition specifically central venous hyperalimentation using hypertonic glucose and amino acids (1970–1975) in the treatment of patients with fistulas. The principal causes for mortality in the historical sense were malnutrition, sepsis and electrolyte imbalance. Mortality among patients with gastrointestinal cutaneous fistulas decreased between the first and second periods from approximately 48 to 15%. Surprisingly, mortality did not decrease further in the "hyperalimentation period" although spontaneous closure of gastrointestinal fistulas increased. The results suggest that the improvement in mortality in patients with gastrointestinal cutaneous fistulas is mostly due to the introduction of improved parasurgical care. It is acknowledged that nutritional support was practiced in the 1960's although this was generally not in the form of hyperalimentation. The addition of hyperalimentation in large scale to the treatment of gastrointestinal cutaneous fistulas has improved spontaneous closure and is a valuable part of the armamentarium. The decrease in mortality however, cannot be attributed to parenteral nutrition.

In 1960, Edmunds, Williams and Welch reviewed their experiences with the treatment of 157 patients with gastrointestinal cutaneous fistulas. In this classic paper they called attention to the serious nature and the high mortality of such fistulas and pointed out the relationship between infection, malnutrition, output and mortality. They also stressed that no patient with a high output fistula with malnutrition survived. In 1964, Chapman, Foran, and Dunphy stressed the importance of good nutritional support and reported a decreased mortality of 14% in those patients treated with an excess of 3,000 calories. The mortality rate in those patients in whom 3,000 calories could not be achieved remained high. It was not until the 1970's with the advent of wide spread parenteral nutrition that overall reduction in mortality to the range of 5–20% was achieved in a variety of papers. Since total parenteral nutrition was widely used, it was suggested that this decreased mortality was due entirely to the provision of adequate nutrition to these patients. The relative merits, however, of total parenteral nutrition, as opposed to general advances of fluid and electrolyte therapy, patient management, increased knowledge of respiratory assistance and physiology, acid base balance as well as increased experience with gastrointestinal fistulas was not established.

In order to achieve a perspective on the relative contributions of total parenteral nutrition as opposed to other advances in parasurgical care, we reviewed patients with gastrointestinal fistulas treated at Massachusetts General Hospital for the decade of 1960–1970 and compared the results achieved in this decade with those of 1970–1975 when total parenteral nutrition was widely used in the treatment of such patients. Surprisingly, mortality rates between 1960 and 1970 was a rather low 15%. In this report, therefore, we compare the mortality and other aspects of treatment of two large series of gastrointestinal fistulas treated at one institution by the same group of surgeons with two entirely different techniques. We hope to show that the principles first enunciated by Edmunds, et al., are still applicable to the treatment of gastrointestinal fistulas. Moreover, it is apparent from this report that the general advances in parasurgical care, *i.e.*, fluid and electrolyte therapy, intensive care patient moni-

* Department of Surgery, University of Limburg, Maastricht, Holland.

† Department of Surgery, University of Cincinnati Medical Center, Cincinnati, Ohio 45267.

Reprint requests to Dr. Fischer.

Submitted for publication: January 2, 1979.

0003-4932/79/0800/0189 $01.20

TABLE 1. *Mortality of Patients with External Gastrointestinal Fistulas (1946–1959)*

Gastrointestinal fistulas	(55)	Mortality	62%
Small bowel fistulas	(46)	Mortality	54%
Large bowel fistulas	(56)	Mortality	16%
Overall Mortality	(157)		43.3%

Mortality of all patients with external gastrointestinal fistulas at Massachusetts General Hospital, Boston, U.S.A. from 1947–1960.

toring, acid base balance, etc., have contributed as much or more as total parenteral nutrition to the overall salvage of these patients.

Clinical Material

The records of 247 patients with gastrointestinal fistulas, all those patients seen between 1960 and 1975 were reviewed retrospectively. These were broken down to 119 patients with gastrointestinal fistulas seen between 1960 and 1970, prior to the widespread use of parenteral nutrition and 128 patients treated between 1970 and 1975. Of these 128 patients in the latter series in which hyperalimentation was widely used, 73 of them were treated with total parenteral nutrition. Somewhat surprisingly, the mortality between 1960 and 1970 was found to be 15%, and the overall mortality between 1970 and 1975 was 21%. Analysis of the data will show that the fistula population has changed and that different factors are responsible for the mortality in these two time periods. In addition, we will try to define what role parenteral nutrition has played and does play in the treatment of gastrointestinal fistulas.

1946–1959 Series (157 Patients with External Gastrointestinal Fistulas) Edmunds, et al.,[8]

Overall mortality (Table 1) amounted to 43.3%. The highest mortality was observed in gastroduodenal fistulas (62%) whereas mortality in colonic fistulas was only 16%.

Surgical complications were the direct cause of 67% of these 157 fistulas. The most significant complications of these fistulas were fluid and electrolyte imbalance, malnutrition, and sepsis. These complications largely determined mortality: 78, 61 and 67% respectively. Despite the advent of antibiotics and modern replacement techniques, the results did not present evidence that these techniques contributed to decreased mortality during the 1946–1959 time period. Since surgical complications were the most frequent cause of external fistulas, prevention was considered essential. For this purpose more widespread use of catheter duodenostomy after gastric resection was recommended. Small bowel fistulas generally were high output fistulas, and early surgical therapy by resection of the fistula and the segment of bowel from which it arises was advocated. Fistulas of the lower bowel had a high incidence of spontaneous closure; expectant treatment was satisfactory in many instances.

1960–1970 Series (119 Patients with Gastrointestinal Fistulas)

One hundred nineteen patients were treated during 139 admissions. Fifty-seven patients were male and 62 female. The mean age was 56 years. In case of multiple fistulas, the fistulas were classified according to their site of primary origin. All gastrointestinal cutaneous fistulas were reviewed, from the esophagus to the rectum. No perianal or perirectal fistulas were included. Both internal and external fistulas and combinations of the two were included in the study. Thirty-one patients had internal fistulas only.

Table 2 lists fistula location and primary disease. The primary disease is either the disease giving rise to a "spontaneous" fistula, or the disease for which the patient was operated on. Striking findings are the low number of gastroduodenal fistulas (15 instances of which two were internal) and the large number of external fistulas due to regional enteritis as compared with the 1946–1959 series. In the 1946–1958 series, small bowel internal fistulas associated with regional enteritis were present in only nine patients.

Table 3 lists the cause of the fistula: the disease itself or the operation or a combination of the two. This categorization is arbitrary, but in daily practice, fistulas occur which are clearly spontaneous, and fistulas are caused exclusively by technical perioperative errors. There is an intermediate category, however, where the likelihood of developing a perioperative fistula is greatly enhanced by the severity of the disease. Therefore, we introduced among "operative injuries" operation and disease-fistulas. The surgical procedures which were considered to be the exclusive cause of fistula formation are listed in Table 4. Eight fistulas were caused by operations for ileus and/or adhesions. Only eight fistulas occurred after gastric operations.

Fistula Complications

Through the decades, the three major complications of fistulas have been: electrolyte disturbance, malnutrition, and sepsis, all primary determinants of mortality. Fistula complications are listed in Table 5.

Malnutrition was present in 104 of 119 patients. Moderate malnutrition was defined as total protein of less than 6 g/100 ml and/or weight loss of greater than 7 kg, and was present in 68 out of 119 patients. Severe malnutrition was defined as a total protein of

TABLE 2. *Primary Disease in 119 Patients (1960–1970) with Gastrointestinal Fistulas*

Fistula Location	Total	Cancer	Ulcer	Chole-cystitis	Pan-creatitis	Diver-ticulitis	Appen-dicitis	Adhe-sions	Trauma	Inflamm. Bowel Disease	Other
esophageal	2	2									
gastric	4	2									2
duodenal	11		5	2	3						1
jejunal	5	1	2					1	1		
ileal	36	11						4		21	
Large bowel											
cecum-											
ascending	8	5					2				1
transverse	11	8		1						1	1
descending	4							1		1	2
rectosigmoid	29	10				14				3	2
Other											
vesical	1	1									
liver	1								1		
gall bladder	2			2							
pancreas	2				2						
vagina	3	3									
Total	119	43	7	5	5	14	2	6	2	26	9

less than 5 g/100 ml and weight loss of greater than 11 kg and was present in 36 out of 104 patients.

Electrolyte imbalance was present in 54 of 119 patients, and surprisingly, occurred in gastroduodenal, small bowel and large bowel fistulas in about equal numbers.

Infection was divided into two subgroups: wound infection in well draining wounds was listed as controlled infection. Sepsis, intra-abdominal abscesses and peritonitis were categorized as uncontrolled infection. Sixty-six of 119 patients had infection. Of these, 30 were regarded as controlled, and 36 as uncontrolled.

Intestinal obstruction was present in 30 out of 119 patients, a somewhat higher figure than in previous series.

TABLE 3. *Etiology of Gastrointestinal Fistulas in 119 Patients (1960–1970)*

Operative Injuries 86		
Operation and disease		30
appendicitis	2	
duodenal ulcer	1	
pancreatitis	3	
regional enteritis	13	
ulcerative colitis	2	
diverticulitis	7	
others	2	
Operation and cancer		8
Operation and cancer and radiation		5
Unknown		1
Operative injury		27
Suture line failure		15
Spontaneous 33		
Cancer		9
Cancer and radiation		3
Regional enteritis		7
Diverticulitis		6
Granulomatous colitis		2
Ulcerative colitis		1
Peptic ulcer		2
Duodenal ulcer		1
Ruptured cholecystitis		2

Indications for Operation (Table 6)

Persistent drainage of the fistula was the most common single indication (33 times) for operation. In 41 other fistula patients, persistent drainage was associated with other indications, like abscesses, peritonitis, obstruction, bleeding of the primary disease itself: inflammatory bowel disease and malignancy.

Operation (Table 7)

Forty-five patients underwent bowel resection with primary anastomosis. In a large number of these cases, ancillary procedures such as abscess drainage, excision of the fistula, etc, were performed. Eighteen pa-

TABLE 4. *Operations Which Caused Gastrointestinal Fistulas in 119 Patients (1960–1970)*

Gastrectomies	6
Persistent gastrectomies	2
Laparotomies for adhesions and ileus	8
Colostomies	4
Persistent cecostomies	5
Colon resections	3
Pancreatectomies	5
Others	9
Total	42

TABLE 5. *Complications of Gastrointestinal Fistulas in 119 Patients (1960–1970)*

	Total	Esophageal Gastric Duodenal	Small Bowel	Large Bowel	Other
Malnutrition	104				
moderate	68	11	24	29	4
severe	36	3	15	15	3
Electrolyte imbalance	54	11	18	21	4
Obstruction	30	3	15	11	1
Bleeding	4	2	2		
Infection	66				
controlled	30	4	17	9	0
uncontrolled	36	5	15	13	3

tients underwent bypass procedures or external diversion, and 13 patients underwent staged operations. Many of these included external diversion or bypass and abscess drainage in association with a later bowel resection and anastomosis.

A small group underwent comparatively minor procedures such as abscess drainage, excision of the fistula and fistula closure, which are not listed in Table 7.

Patients with resection and primary anastomosis showed the highest closure rate. Forty-three of 45 patients were closed in this way. In contrast, bypass or diversion operations failed to obtain closure in five of 18 patients. Staged operations obtained closure in only six of 13. The number of perioperative complications was significantly lower after resection than after bypass-diversion or staged procedures. Only 12 of 45 patients in the resection group sustained major complications such as infections, anastomotic breakdown, etc. Patients with bypass or diversion operations, however, suffered eight complications in 18 patients. Only two of the 13 patients subjected to staged procedures were free of complications.

Closure (Table 8)

Surgical procedures for closure of the fistula were carried out in 96 of all 119 patients (80.7%). Ultimately, 81 fistulas closed (68.1%). Fifteen were operative failures (12.6%). In 12 patients the fistulas closed spontaneously (10.1%).

Total closure rate, therefore, amounted to 78.2%. No attempt at closure was made in 11 patients (9.2%). Seven of these patients died.

Table 9 shows the closure rates in the light of etiologic factors of primary disease. All but one of the 32 patients with inflammatory bowel disease and diverticulitis were operated for their fistulas. Only two fistulas were not closed. These patients died.

The results were far inferior in patients with fistulas due to carcinoma or operative injuries (Table 9), exhibiting a considerable mortality and low closure rate. Only fistulas due to operative injury had a significant spontaneous closure rate (11 of 42).

Closure rate was lower (67.9%) in the group with high-output fistulas than in low or moderate output groups, but the differences were not statistically significant (Table 10).

Much more significant was the relationship between overall closure rate and sepsis (Table 11): closure was

TABLE 6. *Indications for Operation (1960–1970)*

	Total in Group	No.	Esophageal Gastric Duodenal	Small Bowel	Large Bowel	Other
Persistent drainage alone	74	33	8	8	13	4
with abscess/peritonitis		12		5	5	2
+ obstruction		7	1	5	1	
+ bleeding		1		1		
with obstruction		13		3	8	2
+ ileus		1		1		
+ carcinoma		2			2	
with diverticulitis		2			2	
with gastric ulcer		1	1			
with bleeding		1		1		
with diarrhea and pain		1		1		
Abscess or peritonitis	14	7		4	3	
with obstruction		5		2	3	
with bleeding		2	2			
Obstruction	5	2			2	
with wound dehiscence		1		1		
with diarrhea		2		1	1	
Cancer	3	1			1	
with abscess		1			1	
with obstruction		1			1	
Total	96	96	12	33	43	8

TABLE 7. *Types of Operation, Closure and Complication Ratio (1960–1970)*

	No.	Closure		Complications	
		Yes	Failure	None	Yes
Bowel resection	45	43	2	33	12
Bypass/diversions	18	13	5	10	8
Staged procedures	13	7	6	2	11

often unsuccessful in the presence of uncontrolled sepsis: 16 out of 36 patients with uncontrolled sepsis did not close their fistulas and ultimately died.

Mortality (Table 11)

Eighteen out of 119 patients died (15.1%); 10 of these patients died in the presence of carcinoma. Mortality is higher, but not significantly related to increased output (Table 10). A stronger correlation, however, exists between uncontrolled infection and mortality and is inversely related to closure rate. Of 36 patients with uncontrolled sepsis, 11 died, whereas in the controlled infection and no infection group respectively, zero and seven patients died. Three of these seven patients died with carcinoma. Malnutrition also correlated better with mortality than did output (Table 12). As can be expected from these data, sepsis correlates very significantly with malnutrition, with uncontrolled sepsis often associated with severe malnutrition.

1970–1975 Series (128 Patients with Gastrointestinal Fistulas)

Clinical Material

From 1970–1975, 128 patients with gastrointestinal fistulas were treated at Massachusetts General Hospital, of which 73 were treated with total parenteral nutrition, 36 females, 37 males. Six of these 73 patients had associated internal fistulas. Of the 55 patients with fistulas, (27 females, 28 males) which were not treated with total parenteral nutrition, 25 had associated internal fistulas. Fistula location and the disease which caused the fistula or for which the patient was originally operated on are given in Table 13.

In the group treated with hyperalimentation, gastroduodenal and small bowel fistulas predominate. The underlying etiology involves the surgical complications in the overwhelming majority of those patients treated with hyperalimentation (Table 14). In the nonhyperalimented group, most fistulas were large bowel fistulas and of sponaneous nature (Table 14). Considering the entire group of 128 patients, inflammatory bowel disease and cancer (Table 13) were seen most frequently as the underlying disorder, with gastroduodenal ulcer and diverticulitis also figuring prominently.

TABLE 8. *Fate of 119 Patients with Gastrointestinal Fistulas (1960–1970)*

Category	No.	Percentage
Surgical procedures	96	80.7
closed operatively	81	68.1
operative failures	15	12.6
Not operated	23	19.3
closed spontaneously*	12	10.1
no closure (7 of these 11 died)	11	9.2

* All but one were operative fistulas.

TABLE 9. *Closure Rates by Etiology/Primary Disease (1960–1970)*

	Inflammatory Bowel Disease	Diverticulitis	Cancer	Operative Injuries
No. of patients	20	12	26	42
Immediate cause				
spontaneous	7	6	12*	—
operative	13	6	14†	42
Fate				
closed (spontaneous)	1	—	—	11
closed (operative)	18	11	17	22
open	1	1	9	9‡
open (not operated)	—	—	5	4
dead	1	1§	7	6

* Includes 3 following radiation.
† Includes 5 patients in whom operation was preceded by radiation.
‡ Four patients had cancer at fistula.
§ Stayed open.

Fistula Complications (Table 15)

Complications were categorized using the same criteria as in Table 5. The overwhelming number of patients had controlled and uncontrolled infection; only four patients had no infection. Complications in the nonhyperalimented group were far less numerous, and the incidence of uncontrolled sepsis was significantly lower than in the hyperalimented group.

TABLE 10. *Malnutrition, Electrolyte Disturbances, Closure Rate and Mortality, Related to Fistula Output (1960–1970)*

Output (ml/day)	Malnutrition (Per Cent)	Electrolyte Disturbances (Per Cent)	Closure (Per Cent)	Mortality (Per Cent)
>500 (28 patients)	100	86*	67.9	25
200–500 (32 patients)	84.4	50*	78.1	12.5
<200 (28 patients)	71.4	7.1*	82.1	10.7
Internal	93.6	45.2	83.9	12.5

* $p < 0.01$.

TABLE 11. *Infections, Closure Rate and Mortality (119 Patients, 1960–1970)*

Category	No.	Fate		
		Closed	Open	Death
Infection				
controlled	30	28	2	0
uncontrolled	36	20	16	11
No infection	53	44	9	7
Total	119			

Correlation:closure	
uncontrolled versus no infection	$p < 0.01$
uncontrolled versus controlled infection	$p < 0.01$
controlled versus no infection	$p = NS$

Indications for Surgical Treatment (Table 16)

In the hyperalimented group intraperitoneal abscesses, adjacent to or secondary to gastrointestinal fistulas, constituted an important indication for operation. In the nonhyperalimented group, a relatively large group were operated on for the primary disease, rather than for the co-existing fistula.

Operation (Table 17)

In most instances resections were performed, especially in the hyperalimented group, because of the high percentage of small bowel fistulas. In the nonhyperalimented group, consisting largely of patients with large bowel fistulas, approximately half of the operations were bypass–diversion, or staged operations. In many instances, in these operations, ancillary procedures were performed such as abscess drainage, fistula resection, etc. In a small group only drainage, fistula closure or fistula resection was performed.

TABLE 12. *Malnutrition, Infection and Mortality (1960–1970)*

Degree of Malnutrition	Total No. Patients	Controlled Sepsis	Uncontrolled Sepsis	No Sepsis	Mortality
Severe	36	7	17	12	10/36 (27.8%)
Moderate	68	21	18	29	7/68 (10.3%)
None	15	2	1	12	1/15 (6.7%)

Results in 128 Patients with Gastrointestinal Fistulas (Table 18)

Fourteen of the patients (29.2%) that were operated in the hyperalimented group died. Of the patients that were not operated in this group, four died. Almost all patients that were operated in the hyperalimented group had their fistulas closed: only two fistulas stayed open.

Thirty-three of the 48 patients that were operated had their fistulas closed, and survived. In the 25 patients that were not operated in the hyperalimented group, 17 closed their fistulas spontaneously, eight stayed open: four of these eight patients died.

In the nonhyperalimented group 40 out of 55 patients were operated. Four patients died. In 35 of these 40 operated patients, fistula closure was achieved, but two of these died; thus 33 out of 40 operated patients closed their fistulas and survived.

Fifteen patients of the 55 were not operated on. In three patients, spontaneous fistula closure occurred. In 12 patients, fistulas stayed open; five of these patients died. Overall mortality in the 128 patients (1970–1975) amounted to 27 (21.1%), 18 (24.7%) in the hyperalimented group, 9 (16.3%) in the nonhyperalimented group.

TABLE 13. *Fistula Location and Primary Disease (1970–1975)*

Fistula Location	Total	Inflam. Bowel Dis.	Cancer	Ulcer	Cholecystitis	Pancreatitis	Diverticulitis	Appendicitis	Peritonitis	Other
Hyperalimented										
Esophageal	2									2
Gastroduodenal	15	1	1	4	1	1				7
Pancr-Biliary	2			1		1				
Small Bowel	43	16	11	2		1	5	1	1	6
Colon & Rectal	11	4	3				1		2	1
Nonhyperalimented										
Esophageal	5	2	1							2
Gastroduodenal	5			4	1					
Pancr-Bil	3	2								1
Small Bowel	9	7	1						1	
Colon & Rectal	33	6	9				10	1		7
Total	128	34	29	12	2	3	16	2	4	26

TABLE 14. *Fistula Location and Primary Etiology (1970–1975)*

Hyperalimented Patients	Esophageal	Gastro-Duodenal	Pancreatic Biliary	Small Bowel	Large Bowel
Surgical complications	2	13	2	35	7
Persistent gastrostomy drainage		1			
Inflammatory disease		1		7	2
Undetermined				2	1
Total	2	15	2	44	10
Nonhyperalimented Patients	**Esophageal Gastro-Duod.**		**Pancreatic Biliary**	**Small Bowel**	**Large Bowel**
Surgical complications	3			1	6
+ cancer	1		1	1	3
+ diverticulitis					4
+ inflamm. bowel dis.					1
+ stomal ulcer	1				
Inflammatory disease					
Diverticulitis					7
Ulcer disease	2				
Inflamm. bowel disease				7	5
Cholecystitis			1		
Cancer	1		1		7
Trauma	1				1
Total	9		3	9	34

Mortality, Infection and Malnutrition (Table 19)

In the hyperalimented group, 18 patients died. Eleven of these patients had small bowel fistulas. Of these 18 patients, 15 had uncontrolled sepsis; twelve of these patients had pulmonary sepsis. All 12 patients exhibited severe malnutrition and suffered from uncontrolled infection. Four patients died with esophageal–gastroduodenal fistulas. Only one of these patients developed a fistula after an elective procedure for gastroduodenal ulcer disease. Only three patients with colonic fistulas died.

In the nonhyperalimented group uncontrolled infection was also associated with malnutrition and largely determined mortality. Death associated with small bowel fistulas and large bowel fistulas was rare in the nonhyperalimented group. Death associated with esophageal fistulas occurred relatively often in this group: one patient developed a fistula after transthoracic ligation of bleeding esophageal varices, one patient had a bronchoesophageal fistula because of a bronchial carcinoma and one patient developed a fistula after lye ingestion. Only one patient died with duodenal fistula; this patient had carcinoma of the gallbladder.

Discussion

The number of patients with external fistulas admitted during the three time periods was comparable during 1946–1959 and 1960–1970 (Table 20). During 1970–1975, however, a very striking increase in the number of patients treated was observed. This may in

TABLE 15. *Complications of Gastrointestinal Fistulas in 128 Patients (1970–1975)*

	Hyperalimented (73 Patients)					Nonhyperalimented (55 Patients)				
	Esophageal Gastroduod.	Pancreatic Biliary	Small Bowel	Large Bowel	Total	Esophageal Gastroduod.	Pancreatic Biliary	Small Bowel	Large Bowel	Total
Malnutrition	11	3	32	19	65	4	1	3	13	21
Infection										
controlled					30					15
uncontrolled					39					11
Electrolyte imbalance	9	2	21	3	35	2	1	3		6
Obstruction	1	1	3	8	13	1		1	8	10
Bleeding	4	1	6		11		1			1
Wound dehiscence	1	2			3					
Renal failure				1	1					
Jaundice				1	1					

TABLE 16. *Indications for Surgical Treatment* (1970–1975)*

	Esophageal Gastroduod.	Pancreatic Biliary	Small Bowel	Large Bowel
Hyperalimented (73 patients)				
Persistent drainage	2	2	20	5
Intraperitoneal abscess + obstruction	2		15	3
Peritonitis			1	1
Obstruction	1		4	1
Bleeding	2		3	
Disease			1	
Total	7	2	45	10
Nonhyperalimented (55 patients)				
Persistent drainage	2	1	3	14
+ UTI/GUT problems			1	7
Intraperitoneal abscess		1	1	4
Peritonitis			3	
Obstruction			1	5
Disease	2			
Regional enteritis			5	4
Ulcerative colitis				2
Diverticulitis				6
Other	4	1		5
Total	8	4	14	47

* Note: Some patients have more than one indication.

TABLE 17. *Operations for Gastrointestinal Fistulas (1970–1975)*

Type of Procedure	Total	Hyperalimented	Nonhyperalimented
Resection	50	31	19
Bypass/diversion	16	7	9
Staged procedures	7	—	7

part be explained by the increase in the number of patients that were referred to the MGH with existing fistulas. Many of these patients had been hyperalimented at other institutions and failed to close their fistulas: they represent a refractory group, often with uncontrolled sepsis. More aggressive and complicated therapeutic approaches (Table 21) may yield better overall results but may also result in additional complications. Mortality and closure rate (Table 22) improved dramatically during the last two time periods.

1960–1970 Series

It is striking, however, that this decrease in mortality was already achieved in the prehyperalimentation era (1960–1970). It follows that we should be careful in attributing the good results of recent series exclusively to hyperalimentation. We found in the 1960–1970 series that many suggestions put forward in the Edmunds et al. paper proved to be of value.

The low incidence of gastroduodenal fistulas in the 1960–1970 series for instance has eliminated to a large extent these hard to treat high-output fistulas. They will be discussed later in more detail.

Therapeutic results in small bowel fistulas also improved dramatically when compared with the 1946–1959 series. An increasing number of small bowel fistulas were associated with inflammatory bowel disease, often associated with electrolyte disturbances. This did not contribute to mortality however, whereas in the 1946–1959 series, electrolyte disturbances were associated with a mortality of 78%. The time period which elapsed between the genesis of the fistula and the treatment did not correlate with mortality. The fistulas which were due to acute surgical

TABLE 18. *Results in 128 Patients with Gastrointestinal Fistulas (1970–1975)*

	Operative Results	
	Hyperalimented 48 Out of 73 Operated (65.8%)	Nonhyperalimented 40 Out of 55 Operated (72.7%)
Mortality	14 (29.2%)	4 (10%)
Operative closure	34 (70.8%)—1 died	35 (87.5%)—2 died
Operative success (clos. + alive)	33 (78.8%)	33 (82.5%)
	Non-operative Results	
	Hyperalimented 25 Not Operated (34.2%)	Nonhyperalimented 15 Not Operated (27.3%)
Closed spontaneously	17 (68%)	3 (20%)
Stayed open	8 (32%)	12 (80%)
Mortality	4 (16%)	5 (41.7%)
	Hyperalimented	Nonhyperalimented
Overall mortality	18 (24.7%)	9 (16.3%)
Overall closure + alive	50 (68.4%)	36 (65.4%)

TABLE 19. *Mortality in Relation to Infection and Malnutrition (1970–1975)*

	Hyperalimented (73 Patients)	Nonhyperalimented (55 Patients)	Total (128 Patients)
Mortality	18 (24.7%)	9 (16.4%)	27 (21.1%)
Es. gastroduodenal	(17) 4 (23.5%)	(10) 4 (40%)	(27) 8 (29.6%)
Small bowel	(43) 11 (25.6%)	(9) 2 (22.2%)	(52) 13 (25%)
Large bowel	(11) 3 (27.3%)	(33) 3 (9.1%)	(44) 6 (13.6%)
Infection	16	6	22
Controlled	1	—	1
Uncontrolled	15*	6	21
None	2	3	5
Malnutrition	15	8	23
Moderate	3	3	6
Severe	12†	5	17
None	3	1	4
Pulmonary emboli	2		
Myocard infarction	1		
Renal failure	2		
Massive bleeding	2		
Malignancy as associated cause of death.	2	4	

* 4–5 of these patients had ongoing sepsis which was not located in the abdomen but was of pulmonary origin.

† All 12 patients with severe malnutrition had uncontrolled infection. In 4 of these patients, pulmonary infection existed.

catastrophe however were generally operated only a few days after discovery, especially when concomitant sepsis existed. When sepsis was well controlled in surgical catastrophe, spontaneous closure occurred relatively often in this group (26%), especially when one takes into consideration that in the 1960–1970 series no deliberate attempt was made to close fistulas conservatively. The period between discovery and operation was generally longer in stable patients without sepsis with fistulas with low output. In these patients, it seems warranted to wait for spontaneous closure, even without hyperalimentation, this mode of treatment not yet being used in the 1960–1970 patients. This approach explains why mortality does not correlate with output in this time period. For the same reason, malnutrition correlates better with uncontrolled sepsis than with output. It is very clear from the 1960–1970 series that uncontrolled sepsis largely determines mortality. It follows that it is a first priority in the treatment of fistulas to convert uncontrolled sepsis to controlled sepsis, especially as the advent of antibiotics did not improve results in the 1946–1959 series.

The clinical picture displayed by patients with internal fistulas resembled a low-output fistula. Closure rate was high (82.1%) in this group. Mortality was low (12.5%). Malnutrition was high (93.6%), but severe malnutrition low compared with other groups (22.6%). In addition, many of these internal fistulas occur in patients with malignant disease or inflammatory bowel disease, which in itself may cause malnutrition.

The data presented herein once again stress the importance of performing resection and end-to-end anas-

TABLE 20. *Patients with External Gastrointestinal Fistulas Treated at the Massachusetts General Hospital*

Period	Patients Treated	Incidence/ Year	Patients Admitted with Existing Fistulas
1946–1959	157	11.2	28%
Jan. '60–Dec. '70	88	8	30.7%
Dec. '70–Jan. '75	97	24.2	50.5%

TABLE 21. *Factors Influencing Fistula Closure in 55 Fistula Patients (1970–1975) without Hyperalimentation*

	Esoph. Gastro-duod.	Pan-creatic Biliary	Small Bowel	Large Bowel	Total
Cancer	1	2	1	4	8
+ radiation	1			4	5
+ chemotherapy				1	1
+ both	1				1
Regional enteritis			4	1	5
+ steroids			3	3	6
Leukemia					
+ radiation				1	1
+ chemotherapy				1	1
+ steroids				1	1
Lupus erythematodes disseminatus					
+ steroids				1	1
Total					30

TABLE 22. *Closure Rate + Mortality (3 Time Periods)*

	Closure Rate (Fistula Closed, Patient Alive)	Mortality
1946–1959		44%
1960–1970	78.2%	15.1%
1970–1975	62.2%	21.1%

tomoses whenever surgery is undertaken, rather than bypass procedures, partial external diversions and staged procedures. The local situation in the patients in whom bypass or diversion operations were performed may have excluded resection and definitive therapy in some instances. Whenever possible, however, resection and primary anastomosis should be attempted. If this is impossible, total exclusion should be attempted rather than bypass operations or partial exclusions.

The 1960–1970 series has clearly demonstrated that the decreased mortality rate is based upon two aspects:

1) Better patient monitoring including correction of electrolyte disturbances, support of respiratory and cardiac insufficiency.
2) The application of sound surgical principles acquired in the past decades as proposed by Edmunds, et al.[8]

1970–1975 Series

Mortality rates and closure rate still compared very favorably with the 1946–1959 series. Despite hyperalimentation, however, overall closure rate declined and mortality rate increased. Differences were not statistically significant. What was significant was that the advent of hyperalimentation was not associated with an improved closure rate and survival.

It has already been mentioned that the percentage of patients referred to the MGH with existing fistulas increased significantly in the 1970–1975 series. This phenomenon brought about a change in the composition of patient population as reflected in Tables 23–27.

Table 23 demonstrates the increased incidence of fistulas in 1970–1975. This applied especially to the small bowel fistulas. More than half of the patients that were ultimately hyperalimented, were referred with existing fistulas, and these were predominantly small bowel fistulas. Most of these patients had been hyperalimented at other institutions. In the nonhyperalimented group, only a third was referred.

TABLE 23. *Fistula Locations in 1960–1970 Series and in Hyperalimented and Nonhyperalimented Groups from 1970–1975*

	Totals 1960–1970	Totals 1970–1975	Hyperalimented 1970–1975	Nonhyperalimented 1970–1975
Esophageal	2	7	2	5
Gastroduodenal	15	20	15	5
Pancr-Biliary	4	5	2	3
Small bowel	41	52	43	9
Colorectal	52	44	11	33
Others	5	—		
Total	119	128	73	55

In 1970–1975, a substantial increase in the number of patients with fistulas due to inflammatory bowel disease was observed (Table 24). It is also striking, however, that in the 1970–1975 period, more fistulas[16] due to diverticulitis of the colon were observed than in the longer 1960–1970 period.

Table 25 compares etiology. Apart from the increase in incidence, there seems to be a relative decrease in fistulas due to surgical complications. This is reflected in an increase in spontaneous fistulas due to inflammatory disease which comprises inflammatory bowel disease and diverticulitis, cholecystitis, ulcer disease, etc.

Fistulas of patients that were hyperalimented were in large proportion due to surgical complications (80.8%) whereas in the nonhyperalimented series, only 40% were considered to be caused by surgical complications. It may be significant (Table 20) that the incidence of malnutrition decreased in the 1970–1975 series from 87% (1960–1970) to 51% (1970–1975). This decrease was observed despite the increase in mortality. That it remained so high as it did despite hyper-

TABLE 24. *Primary Disease*

	Total	I.B.D.	Ca	G.D. Ulcer	Chol.itis	Pan.itis	Divertic.	App.	Perit.	Adhes.	Trauma	Other
Total '60–'70	119	26	43	7	5	5	14	2		6	2	9
Total '70–'75	128	34	29	12	2	3	16	2	4			26
Hyperalimented '70–'75	73	21	15	7	1	3	6	1	3			16
Nonhyperalimented '70–'75	55	13	14	5	1	—	10	1	1			10

TABLE 25. *Etiology*

	Total 1960–1970	Total 1970–1975	Hyperalimented 1970–1975	Nonhyperalimented 1970–1975
Surgical complications	86 (72.2%)	81 (63.3%)	59 (80.8%)	22 (40%)
Spontaneous inflammatory disease	21	32	10	22
Ca	12	9	—	9
Others	—	6	4	2
Total	119	128	73	55

alimentation may be explained by the increased incidence in infection, especially in the hyperalimented group. The low incidence of complications in the nonhyperalimented group is based on patient selection: evidently, only patients with major complications like malnutrition or infection were considered for hyperalimentation. It has been previously noted, however, that the nonhyperalimented group largely consisted of large bowel fistulas, many of these being spontaneous in nature.

Electrolyte imbalances were a major problem in the initial series[8] and contributed to mortality in a major way. Electrolyte imbalance did not result in significant mortality in 1960–1970 or 1970–1975.

The increase in infectious complications rate in the 1970–1975 series is also reflected in the large number of patients that were operated for abscesses secondary to fistulas (Table 27). This especially applies to the hyperalimented group, 23 out of 73 patients (31.5%) being operated on for abscesses. The categorization of indications for operation at times may have been arbitrary because it was not always clear from the records if the abscess preceded the fistula or vice versa. Some patients had an abscess drained following surgery, which was an early manifestation of anastomotic breakdown. In Table 27 we list only those abscesses that developed or remained subsequent to the development of a fistula.

The proportion of staged procedures declined even further in the 1970–1975 time period (Tables 7 and 17). In the majority of operations, early resection with or without primary anastomosis was carried out, probably reflecting lessons learned from previous papers.[8]

Table 28 compares overall results in the two later series.

Gastroduodenal Fistulas

Table 29 summarizes the number of patients with gastroduodenal fistulas in three different time periods. The decrease in the number of fistulas after gastrectomy is noteworthy.

From 1960–1975, 19 patients with gastroduodenal fistulas secondary to neoplastic or ulcer disease were treated. Of these, four were internal, (internal fistulas were not considered in the 1946–1959 series) and two were admitted with existing fistulas, and 13 patients developed their fistulas after some type of gastrectomy performed in the MGH. From 1960–1975, 2150 gastrectomies were performed. Therefore, 0.6% of the patients that underwent some form of gastrectomy from 1960–1975 in the MGH developed a gastric, duodenal or gastrojejunal fistula. This incidence is consid-

TABLE 26. *Fistula Complications*

	1960–1970	1970–1975	Hyperalimented 1970–1975	Nonhyperalimented 1970–1975
Total	119 (100%)	128 (100%)	73 (100%)	55 (100%)
Malnutrition	104 (87%)	65 (51%)	44 (60%)	21 (38%)
moderate	68 (57%)			
severe	36 (30%)			
Infection	66 (55.5%)	95 (74%)	69 (94.5%)	26 (47%)
controlled	30 (25%)	45 (35%)	30 (41%)	15 (27%)
noncontrolled	36 (30%)	50 (39%)	39 (53.4%)	11 (20%)
Electrolyte imbalances	54 (45%)	35 (27%)	29 (40%)	6 (11%)
Obstruction	30 (25%)	13 (10%)	3 (4%)	10 (18%)
Bleeding	4 (34%)	10 (8%)	10 (13.7%)	—
Wound dehiscence		4 (3%)	3 (4%)	1 (1.8%)
Renal/hepatic failure		2 (1.6%)	2 (2.7%)	—

TABLE 27. *Indications for Operation**

	1960–1970	1970–1975 Total	1970–1975 Hyperalimented	1970–1975 Nonhyperalimented
Persistent drainage + ancillary indication	74	57	29	28
Intraperitoneal abscess + ancillary indication	14	32	23	9

* Only numbers for persistent drainage and abscess drainage are given.

erably lower than the 1.4% reported by Edmunds, et al.,[8] in the 1946–1959 period. This may have contributed significantly to the decrease in mortality that is observed in the later time periods, because these fistulas are hard to treat and exhibit a high mortality. Probably, the main reason for the decreased incidence of fistula formation after gastrectomy is the liberal use of catheter duodenostomies as advocated by Rodkey and Welch.[3,8,9,16,17]

Besides a decreased incidence, a decreased mortality was equally observed in the entire group of esophageal–gastroduodenal fistula patients in the 1970–1975 series (Table 19). Mortality dropped from 62% in 1946–1959 to 40% in the nonhyperalimented patients (1960–1970) to 23.5% in the hyperalimented patients in 1970–1975 suggesting that total parenteral nutrition may have contributed to a decrease in mortality.

Small Bowel Fistulas

Coinciding with the decrease in the relative incidence of gastroduodenal fistulas, an increase in incidence of small bowel fistulas occurred. Fifty-two patients out of a total of 128 had small bowel fistulas. Mortality in this group being a substantial 25%, almost half of all patients dying from fistula disease had small bowel fistulas. Almost all of these patients had uncontrolled infection and some degree of malnutrition which undoubtedly contributed to the high mortality observed. Infectious complications in small bowel fistulas in our material do seem to be less amenable to medical or surgical treatment than fistulas in the proximal or distal gut.

Once local peritonitis exists, resection of a diseased segment containing fistula, etc. does not seem to alleviate infection as often in the small bowel as in other parts of the gut. Anastomoses performed in such areas are inclined to break down, small bowel proximal to diseased resected areas may remain distended and a-functional. In some instances, this leads to a vicious cycle: distension causes permeability of the small bowel, leading to some degree of local peritonitis leading to distension and adynamic ileus, etc. Such patients tend to remain septic, develop sequential organ failure and finally die, despite medical and surgical treatment. At autopsy, general peritonitis and unresolved abscesses are found. Not infrequently, however, findings are less conspicuous, representing bowel distension with sometimes only discrete microscopic signs of chronic inflammation.

Large Bowel Fistulas

Large bowel fistulas, once established, showed far fewer complications than fistulas in other parts of the gut. This is in agreement with previous experiences as reported in the literature.[1,2,10,13–15,18] These fistulas generally are of a low output type and cause little or no malnutrition. In addition, abscesses, peritonitis, etc., if present, are generally localized and amenable to surgical therapy. Obstruction occurred relatively

TABLE 28. *Results of Operative and Non-operative Approaches in the Two Latter Series*

	1960–1970	1970–1975	1970–1975 Hyperalimented	1970–1975 Nonhyperalimented
Operative				
Surg. procedures	96	88	48	40
Closed operatively	81	69 (3*)	34 (1*)	35 (2*)
Failed operatively	15	5	2	3
Mortality	11	18	14	4
Operative success (closure + alive)	81	66	33	33
Non-operative				
Spontaneous closure	12	20	17	3
No attempt at closure	11 (7*)			
Stayed open		20	8	12
Mortality	7	9	4	5
Overall mortality	18 (15.1%)	27	18	9
Overall closure + alive	93 (78.2%)	86 (67.2%)	50	36

* Patients with carcinoma.

TABLE 29. *Gastroduodenal Fistulas (1946–1975)*

	Ca	Ulcer	Chol.itis	Pancr.itis	Other	Total
1956–1959	8	38	2	3	4	55
1960–1970	3	7	2	3	5	20
1970–1975	1 (1 + 0)	8 (4* + 4)	2 (1 + 1)	1 (1 + 0)	8 (8 + 0)	20 (15 + 5)

* Including 2 internal fistulas.
Numbers of gastroduodenal fistulas in three different time periods. Between brackets, the number of patients that were hyperalimented and were not hyperalimented respectively (1970–1975).

infrequently in this group, but takes longer to develop and are amenable to surgical therapy.

Consequently, mortality in this group improved only slightly in the 1970–1975 series (13.6%) when compared to a mortality of 16% in the 1946–1959 series.

Only 11 out of 44 patients (1970–1975) required parenteral nutrition for malnutrition, largely associated with septic complications.

Three of these 11 patients died (one with intraperitoneal sepsis and pulmonary embolism, one with intraperitoneal sepsis and renal failure, one due to myocardial infarction).

Factors Determining Mortality and the Influence of Parenteral Nutrition

Through the decades, malnutrition, electrolyte disturbances, and sepsis have determined mortality in patients with enterocutaneous fistulas. Malnutrition and electrolyte disturbances were commonly encountered in patients with high-output fistulas. Advances in patient monitoring, correction of fluid and electrolyte imbalance and parenteral nutrition have largely alleviated malnutrition and electrolyte disturbances secondary to high-output fistulas. In the present era, mortality is largely determined by uncontrolled sepsis and sepsis-associated malnutrition (Table 19), as malnutrition in the group of fistula patients that died (Table 19) was in most instances secondary to uncontrolled sepsis. Only very few patients died exclusively of other causes (Table 19).

Parenteral nutrition has been very effective in treating malnutrition when no uncontrolled sepsis coexisted, as no patients were considered to have died from malnutrition alone. However, malnutrition in the presence of uncontrolled sepsis *cannot* be treated by total parenteral nutrition without effective surgical drainage. So long as uncontrolled sepsis persists, the patient's condition deteriorates. Patients get weaker, become passive, cannot clear lung secretions, develop decubitus ulcers, become edematous, develop neurologic disorders, etc., despite parenteral nutrition. Finally, sequential organ failure develops and death ensues.

In conclusion, the one major determinant of mortality in 1970–1975 is uncontrolled sepsis and it is our impression that total parenteral nutrition does not alleviate this problem. On the contrary, papers[1,3,15] reporting excellent results with conservative treatment of fistulas with total parenteral nutrition should be interpreted carefully because the casual reader might get the wrong impression that as soon as a caval catheter is in place, and a glucose-amino acid mixture is administered, he can turn his back on the patient. All authorities would agree, that this is not the proper approach.

Uncontrolled sepsis should be attacked as early as possible and surgically.[12]

The role of antibiotics remains to be elucidated. Edmunds et al. suggested that antibiotics did not have a major impact on the results during the 1946–1959 era. This impression is confirmed in the two later series. It is our impression from the 1960–1970 and 1970–1975 series that the therapeutic use of antibiotics for intra-abdominal sepsis should be carefully reserved for: septicemia and cholangitis and as preparation for operation. Once signs of intra-abdominal sepsis have occurred, the use of antibiotics do not obviate the necessity to treat the intra-abdominal sepsis surgically.

When sepsis is controlled, or when no sepsis is present, total parenteral nutrition will result in good nutritional status, allowing skin lesions to heal and the future operative field to become quiescent. If spontaneous closure does not occur, operation may then involve less risk than when undertaken in a malnourished patient. Only very few patients died of other causes than uncontrolled infection and associated malnutrition. This demonstrates that total parental nutrition has been effective in treating malnutrition when no uncontrolled sepsis coexisted, because no patients were considered to have died from malnutrition alone. Apart from preparing patients for operation, total parenteral nutrition and bowel rest may achieve spontaneous closure of fistulas. This is most likely to occur when no uncontrolled infection exists, and when we are dealing with well draining lateral fistulas. End fistulas self evidently will not close spontaneously. In addition, distal obstruction, poor condition of the bowel or abscesses adjacent to the fistula constitute reasons for planning a surgical attack on the fistula.[10]

References

1. Aquirre, A., Fischer, J. E. and Welch, C. E.: The Role of Surgery and Hyperalimentation in Therapy of Gastrointestinal-cutaneous Fistulae. Ann. Surg., 180:393, 1974.
2. Ali, S. D. and Leffall, L. D.: Management of Ecternal Fistulas of the Gastrointestinal Tract. Am. J. Surg. 123:535, 1972.
3. Austen, W. G. and Baue, A. E.: Catheter Duodenostomy for the Difficult Duodenum. Am. J. Surg., 160:781, 1964.
4. Bartlett, M. K. and Lowell, W. H.: Acute Postoperative Duodenal Fistula. Am. J. Surg., 218:587, 1938.
5. Bowling, J. W., Hardy, J. D. and Conn, J. H.: External Alimentary Fistulas. Am. J. Surg., 103:6, 1962.
6. Chapman, R., Foran, R. and Dunphy, J. E.: Management of Intestinal Fistulas. Am. J. Surg., 108:157, 1964.
7. Dudrick, S. J., Wilmore, D. W., Vars, H. M. and Rhoads, J. E.: Long Term Total Parenteral Nutrition with Growth, Development and Positive Nitrogen Balance. Surgery, 64:134, 1968.
8. Edmunds, L. H., Williams, G. M. and Welch, C. E.: External Fistulas Arising from the Gastrointestinal Tract. Ann. Surg., 152:445, 1960.
9. Friedemann, M.: Ueber Hilfen und Sicherungen bei gefahrvollen und technisch schwierigen Magenoperationen. Beitr. Klin. Chir., 163:293, 1936.
10. Fischer, J. E.: The Management of High-output Intestinal Fistulas. Adv. Surg., 9:139, 1975.
11. Fischer, J. E., Foster, G. S., Abel, R. M., et al.: Hyperalimentation as Primary Therapy for Inflammatory Bowel Disease. Am. J. Surg., 125:165, 1973.
12. Lorenzo, G. A. and Beal, J. M.: Management of External Small Bowel Fistulas. Arch. Surg., 99:394, 1969.
13. McPhayden, Jr., B. V. and Dudrick, S. J.: Management for Gastrointestinal Fistulas with Parenteral Hyperalimentation. Surgery, 74:100, 1973.
14. Nassos, T. P. and Braasch, J. W.: External Small Bowel Fistulas. Surg. Clin. North Am., 51:687, 1977.
15. Sheldon, G. F., Gardiner, B. N., Way, L. W. and Dunphy, J. E.: Management of Gastrointestinal Fistulas. Surg. Gynecol. Obstet., 51:687, 1971.
16. Welch, C. E.: Surgery of the Stomach and Duodenum. Chicago Year Book, 1955.
17. Welch, C. E. and Rodkey, G. V.: Method of Management of Duodenal Stump after Gastrectomy. Surg. Gynecol. Obstet. 98:376, 1954.
18. West, J. P., Ring, E. M., Miller, R. E. and Burks, W. P.: A Study of the Causes and Treatment of External Postoperative Intestinal Fistulas. Surg. Gynecol. Obstet., 113:490, 1961.